PRELIMINARY OBSERVATIONS ON A CASE OF PHYSIOLOGICAL ALBUMINURIA

BY

TORALD SOLLMANN, M. D., AND E. C. McCOMB

(FROM THE PHYSIOLOGICAL LABORATORY OF THE MEDICAL DEPARTMENT OF WESTERN RESERVE UNIVERSITY, CLEVELAND)

FROM
THE JOURNAL OF EXPERIMENTAL MEDICINE
VOL. III, No. 1, 1898

PRELIMINARY OBSERVATIONS ON A CASE OF PHYSIOLOGICAL ALBUMINURIA.

By TORALD SOLLMANN, M. D., and E. C. McCOMB.

(From the Physiological Laboratory of the Medical Department of Western Reserve University, Cleveland.)

Plate XIII.

Introductory. Usually physiological albuminuria is of the kind designated by Pavy as "cyclic," *i. e.* albumin in notable quantity is at times present, at times absent. This form has been frequently studied and the conditions influencing it are fairly well known. Instances of this kind are undoubtedly physiological.

The present case belongs to the much rarer form, which stands on the very boundary of the physiological and pathological. It was characterized by the constant presence in the urine of a considerable quantity of coagulable proteids, for a considerable length of time, without any other symptoms of general or renal disease.

In February, 1896, one of us accidentally discovered the presence of albumin in his urine. He was at the time in perfect health. A physical examination, made by Prof. C. F. Hoover, failed to disclose anything abnormal. Nor did the ophthalmoscope reveal any trace of albuminuric retinitis. Chemical tests made at intervals since that time have always shown albumin. Frequent microscopical examinations have failed to reveal casts. The state of health at the present date (January, 1898) is still perfect, and there are absolutely no other signs pointing to the presence of renal disease. The weight is 154 lbs., height 5 feet 8 inches, age 27 years.

General Considerations. In view of the comparative uncertainty of our knowledge of the mechanism of urinary secretion, it seems to us that any contribution which could possibly throw some light upon the question would be valuable. The study of the conditions which influence the quantity of the normal urinary constituents has already

yielded good results in this direction, but little has as yet been done in the way of making similar quantitative observations on the conditions influencing the excretion of proteids. The study of the present case therefore seemed to us of interest in this connection, as well as serving as a contribution to the knowledge of the different forms of albuminuria and the causes from which they result. In the present paper we content ourselves with giving the results of our work without attempting to apply them to the general questions suggested, as we are well aware that the number of observations is not sufficiently large nor are the results sufficiently unequivocal. The former defect we hope to remedy in the future. A table and a chart (Plate XIII) at the end of the article present the results of the observations.

The special questions which we attempted to answer are:

1. What is the nature of the proteids in the urine?

2. Is the albuminuria due to some general metabolic change or is it of renal origin?

3. What quantitative variations do the proteids undergo?

1. What is the Nature of the Proteids?

The proteid was found to consist of albumin and globulin. We at first attempted to determine the relative amount of these two substances, both by Pohl's and by Hammersten's method, but no satisfactory results were obtained, probably because the quantity of globulin was too small. We therefore contented ourselves with the estimation of the total coagulable proteid.

After the removal of the coagulable proteids the urine was frequently tested with sodium hydrate and cupric sulphate, but we could never obtain a biuret reaction, showing the absence of notable quantities of non-coagulable proteids.

2. Is the Albuminuria of Metabolic or of Renal Origin?

We attempted to answer this question by varying, as best we could, the conditions ordinarily accepted as influencing the general metabolism and the functional activity of the kidneys. Thus we examined the influence on the quantity of proteid excreted: *a*, of diet; *b*, of

temperature; *c*, of sleep; *d*, of diuretics; *e*, of drugs acting upon the circulation; *f*, of spontaneous variations in the volume of the urine.

a. The effect of diet. The fact that the person under observation eats a good deal of meat and little carbohydrate served to direct our attention to this point.

It will be seen from the tables and curves annexed that, on the whole, the proteids in the urine vary directly as the proteids in the diet, *e. g.* urinary proteids from February 9 to 12 (with a diet poor in proteids) average .5384 grm. per diem; from February 13 to 14 (with a diet rich in proteids), .6430 grm. On closer examination it will be seen that the changes in the urinary proteids only appear the day after the change in the diet. Taking this into account, we have for diet poor in proteids (February 10 to 12) .4465 grm.; for diet rich in proteids (February 14) .6748 grm. The average of the preceding week (with normal diet) was .5083 grm. And on the whole the curves of urea and of coagulable proteids from February 9 to 19 will be found to correspond very closely.

But on the other hand, when we tried to keep the diet approximately uniform in quantity and quality (from February 25 to March 4), large variations were seen in the urinary proteids, which do not at all correspond to changes in the amount of urea.

b. The effect of temperature. The influence of external temperature can be well studied from the chart, in which the average and in some cases the minimum daily temperatures are given (from records of the U. S. Meteorological Station, Cleveland). It will be seen that, as a rule, the coagulable proteids in the urine vary inversely as the temperature, and this in a very striking manner (January 23 to February 6; March 11 to 23; April 14 to 22). Equally striking is the steady decline in the average daily excretion per month from January to April (see below under 3).

Occasionally, however, there are changes in temperature without corresponding changes in the quantity of excreted proteids (April 7 to 14). Or the changes may even be in the same direction in both (February 6 to 8, April 25 to 27); but here the periods were only of two days, and the results could easily have been influenced by other

conditions which escaped observation. A cold sponge-bath of 10 minutes' duration (April 25 and 26) produced no rise in the amount of urinary proteids.

c. Influence of sleep. To determine the influence of sleep (rest and position?), we compared the average hourly excretion of proteids during the day and night, with the following results:

		Quantity of urine.	Quantity per hour.	Per cent. proteids.	Proteids per hour in grms.
April 6 to 7	Day.....	570 cc.	38 cc.	.0520	.0198
	Night....	340	37.8	.0329	.01255
April 14 to 15 ..	Day.....	950	67.9	.0402	.0273
	Night....	370	37	.0557	.0206

It will be seen that during sleep the excretion of coagulable proteid is very notably diminished.

It would have been well to try the effect of severe exercise in this connection, but circumstances did not permit it at the time.

d. Influence of diuretics. In attempting to investigate the part which the kidneys played in the production of this albuminuria we tried (March 11 to April 9) the exhibition of various diuretics, viz. potassium nitrate, potassium acetate, caffeine, and urea, as a method of affecting the renal epithelium. On the whole these diuretics tended to cause a slight rise in the quantity of proteid excreted, but the effect was small and not always to be obtained. Even a dose of 31 grm. of potassium acetate produced very little change.

e. The influence of drugs acting upon the circulation. We chose trinitrin and digitalis for these experiments. The drugs were pushed until their effects were plainly felt. As will be seen from the curves, they tended to increase the excretion of proteid to some extent, but whether this action was due to changes in the renal circulation or to more general vascular effects, or to changes in the metabolism throughout the body or in some particular organ, the evidence at our command does not enable us to decide.

f. The relation between the quantity of urine and the quantity of proteids excreted. As we have seen, when the quantity of urine

is increased by diuretics that act chiefly on the renal epithelium there is little change in the quantity of excreted proteid, but what there is is in the direction of a rise. The same is true of changes produced by diuretics acting chiefly on the circulation. But for those changes in the volume of the urine which, for want of a better name, we may call spontaneous, the case appears to be different, the total proteids sometimes increasing as the quantity of urine diminishes, and sometimes varying directly as the quantity. Thus, in looking at the curves from January 29 to February 6, a period during which no drugs were administered, one cannot fail to be struck with the fact that the maxima of the proteid curve correspond with the minima of the curve representing the changes in the quantity of the urine. From January 25 to January 29, on the other hand, the two curves run parallel. It may be of interest to mention in this connection that the observed individual was unable to drink large quantities of liquid.

3. What Quantitative Variations do the Proteids Undergo?

As will be seen from the curves, the variations in proteids during the three months covered by our observations were comparatively small, much smaller than we expected. The quantity in the twenty-four hours fell once to .2592, and once to .3242, and rose once to .9010, and three times it lay between .814 and .855, but did not stay at any of these extremes longer than one day.

Excluding these exceptional results, we found that the proteid varied from .7 to .37 grm. in 24 hours.

The average in January (10 days) was .6616; February (23 days), .5419; March (16 days), .5111; April (18 days), .4651.

The average for the 67 days observed was .5318 grm. On the supposition, which appears legitimate, that the average daily output for each month was approximately the same as the average of the days actually observed in that month, the daily average for the four months over which the observations extended would be .5449.

Summary.

1. The proteids consisted of albumins and globulins, varying in quantity between the extremes of .9010 grm. and .2592 grm. in the

24 hours, but usually between .7 and .37 grm., the average being .5317 grm.

2. The quantity of the proteids varies directly as the urea, inversely as the external temperature. The relation between the quantity of urine and the quantity of proteid is not constant. The quantity of the proteids is little affected by diuretics; it tends to be increased by certain drugs that act upon the circulation. It is lessened during sleep.

It is apt to suffer a sudden temporary increase, returning as suddenly to the usual average. For this phenomenon we have no explanation.

3. From .5449 to .6616 grm. of coagulable proteids a day (.0079 to .0094 grm. per kilo of body-weight) may be excreted through the urine for an indefinite time by an otherwise healthy individual without damage to either kidneys or organism.

NOTE.

The method employed for the estimation of proteids was the usual gravimetric method with heat precipitation. It was found that the addition of acetic acid, even when done as carefully as possible, detracted from the exactness of the result, and with these urines it was generally quite unnecessary. The method as carried out consisted in heating a certain quantity (usually 100 cc.) of the urine on the sand-bath, bringing to the boil about five times, filtering through ashless filter paper, again boiling the filtrate, cautiously adding a few drops of 2 per cent. acetic acid, and, if this produced any turbidity (which it rarely did), refiltering and repeating the process until all the proteid was precipitated. The precipitate was washed on the filter with distilled water until chlorine-free, then with alcohol, and was dried at 110° C.

As the weather was very cold during the greater part of the time, we usually analyzed the urines of two successive days at the same time. In a few cases we added a small quantity of salicylic acid. Most of the analyses were made on the mixed urine of 24 hours, but some on the mixed urine of 48 hours. All the determinations were made in duplicate, and of course the higher of the two accepted. The difference between the two determinations averaged in 52 cases 3 milligrammes per 100 cc.; in four cases it was between 10 and 11 mg. per 100 cc.

TABLE OF RESULTS.

Date.	Quantity proteid.	Quantity urine.	Sp. gr. urine.*	Average daily temp.° C.	Urea.	Solids of urine calculated by Haeser's coefficient.	Remarks.
5 p. m. to 5 p. m. Jan. 19–20				(20)—3.3			
21				(21)—0.7			
22	.6045	930	27.5	—2.3		59.59	
23	.6045	930	27.5	—9.7		59.59	
24	.7357	880	28	—13.4		58.72	
25	.7357	880	28	—21.4		58.72	
26	.8397	1143	27	—18.7		69.21	
27	.8397	1143	27	—15.2		69.21	
28	.6000	750	29	—15.5		50.68	
29	.6000	750	29	—10.3		50.68	
30	.5279	1025	29	—8.4		69.26	
31	.5279	1025	29	—7		69.26	
Feb. 1	.4486	925	26	—2.8		56.05	
2	.4486	925	26	—2.3		56.05	
3	.6136	800	27	—2.3	23.276	50.72	
4	.6136	800	27	—2.3	23.276	50.72	
5	.4767	965	26	+0.3	29.734	59.05	
6	.4767	965	26	+1.9	29.734	59.05	
7	.4640	950	26	+0.4	28.781	57.56	
8	.4640	950	26	—1	28.781	57.56	
9	.8141	835	28	—1.7	27.791	54.47	Diet poor in proteids, rich in carbohydrates.
10	.4554	990	24	—1.8	20.766	55.36	Diet poor in proteids, rich in carbohydrates.
11	.4092	790	26	—3.3	20.648	47.86	Diet poor in proteids, rich in carbohydrates.
12	.4749	1060	23	—1.9	25.487	56.80	Diet normal in proteids, poor in carbohydrates.
13	.6111	970	24	—2.9	30.705	54.24	Rich in proteids, poor in carbohydrates.
14	.6748	1165	24	+1.9	34.281	65.14	Normal.
15	.7055	850	25	—0.2	30.517	43.49	Poor in both.

*Only the last two figures of the specific gravity, as expressed in the ordinary way, are given.

TABLE OF RESULTS.—*Continued.*

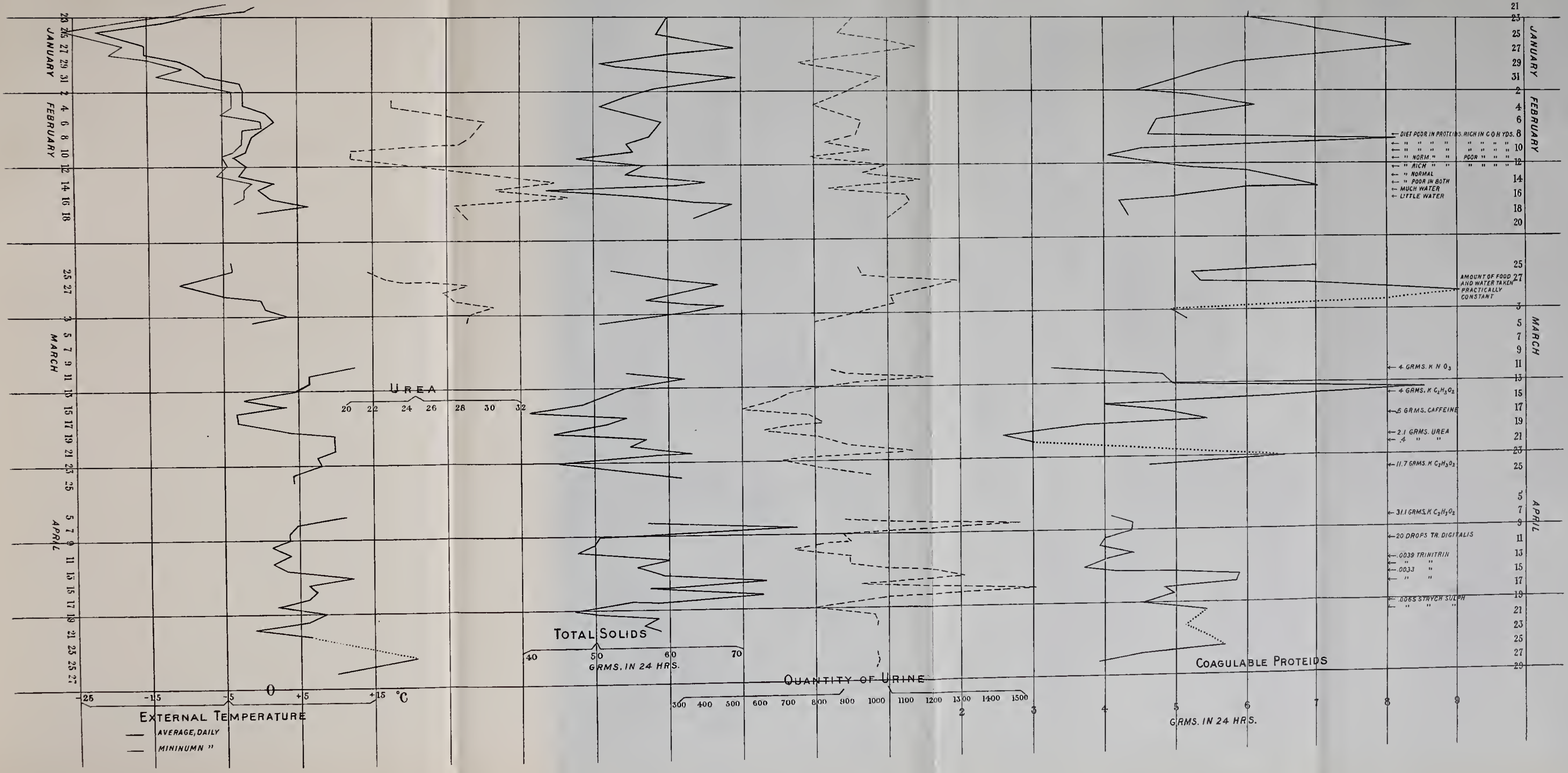
Date.	Quantity proteid.	Quantity urine.	Sp. gr. urine.	Average daily temp. ° C.	Urea.	Solids of urine calculated by Haeser's coefficient.	Remarks.
5 p. m. to 5 p. m.							
Feb. 16	.5197	1120	22	(16)+1	35.189	57.41	Much H_2O taken.
17	.4233	1135	26	+6.6	27.523	68.76	Little " "
18	.4368	1050	26	—0.3	28.355	63.61	
19	.4368	1050	26		28.355	63.61	
25	.7040	950	23.5	—3.6	21.780	52.01	
26	.5251	960	26	—7.8	24.027	58.16	
27	.5330	1300	22	—10.9	28.449	66.64	
28	.7360	1150	23	—7.5	26.838	61.63	Amount of food and water taken practically constant.
to March 1	.9010	1070	23	0	27.459	57.34	
2		1080	27	0.5	30.332	67.94	
3	.4963	960	27	3.3	28.541	60.39	
4	.5184	800	27	—1.1	28.472	50.72	
8 a. m.				(9) 12.2			
to Mch. 11	.3242	860	27	(10) 6.7		54.10	
12	.4828	1210	22	6.7		62.02	4 grm. pot. nitrate taken.
13	.4922	850	27	4.4		53.48	
14	.8554	720	30	—2.2		50.33	
15	.6296	660	31	2.8		48.33	4 grm. pot. acetate.
16	.4015	550	32	—3.3		41.01	
17	.4905	780	30	—3.3		54.52	
18	.5420	825	27	1.6		51.90	.6 grm. caffeine.
19	.3660	630	30	10		44.04	
20	.2592	810	30	10		56.62	
21	.3003	910	26	10		55.13	2.1 grm. urea taken.
22		1090	25	7.2		63.49	.4 grm. urea "
23	.6541	690	28	7.8		45.01	

TABLE OF RESULTS.—*Continued.*

Date.	Quantity proteid.	Quantity urine.	Sp. gr. urine.	Average daily temp.° C.	Urea.	Solids of urine calculated by Haeser's coefficient.	Remarks.
7 a. m.							
to Mch. 24	.4633	820	28	(23) 2.2		53.50	
25		980	27	2.2		61.65	11.7 grm. pot. acet.
				(5) 11.1			
to April 7	.4093	910	27	4.4		57.25	
8	.4408	1520	22	3.3		77.91	31.1 grm. pot. acetate.
9	.4392	900	24	3.3		50.33	
10	.3999	930	23	1.1		49.84	
11	.3927	730	28	3.3		47.63	20 min. tr. digitalis.
12	.4407	920	28	1.1		60.02	
13	.3993	920	26	3.3		55.74	
14	.3696	1200	21	12.2		58.79	.0039 grm. trinitrin.
15	.5880	1320	23	6.1		73.82	" " "
16	.5852	950	26	7.2		57.55	.0033 " "
17	.4804	1570	20	6.1		73.16	" " "
18	.4970	1000	23.5	1.6		54.75	
19	.4520	800	25	8.9		46.60	
20	.5440	1000	25	6.1		58.25	.0065 grm. strychnin [sulph.
21		1010	24	—1.1		56.48	.0065 " " "
22	.5131	1010	25	6.7		58.83	
25	.5694	1010	26	21.1		61.19	
26	.4567	1015	24	15.6		56.78	Cold sponge-bath, about 10 min., morn. of 25th.
27	.3949	1010	25	10.		58.83	

DESCRIPTION OF PLATE XIII.

See the text.


JANUARY
FEBRUARY
MARCH
APRIL
UREA
TOTAL SOLIDS
GRMS. IN 24 HRS.
QUANTITY OF URINE
COAGULABLE PROTEIDS
GRMS. IN 24 HRS.
EXTERNAL TEMPERATURE
AVERAGE, DAILY
MININUMN "
°C
DIET POOR IN PROTEIDS, RICH IN C.O.H.YDS.
NORMAL
POOR IN BOTH
MUCH WATER
LITTLE WATER
AMOUNT OF FOOD AND WATER TAKEN PRACTICALLY CONSTANT
4 GRMS. K N O3
4 GRMS. K C2H3O2
.5 GRMS. CAFFEINE
2.1 GRMS. UREA
11.7 GRMS. K C2H3O2
31.1 GRMS. K C2H3O2
20 DROPS TR. DIGITALIS
.0039 TRINITRIN
.0033
.0065 STRYCH. SULPH.